

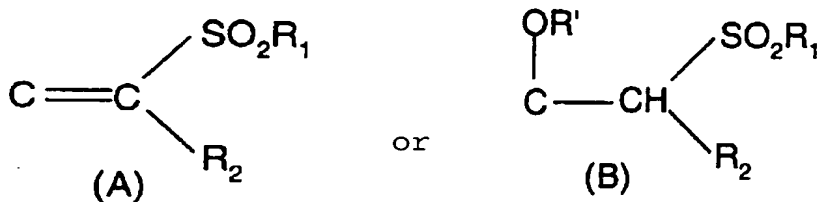
CLAIMS

1. A combination of one or more products which
 activate dopaminergic neurotransmission in the
 5 brain and of one or more CB1 antagonist azetidine
 derivatives of formula (I):



10 wherein

R is a moiety of the formula (A) or (B):



R₁ is methyl or ethyl;

- 15 R₂ is either aryl chosen from phenyl, naphthyl or
 indenyl, wherein the aryl being unsubstituted
 or substituted by one or more halogen, alkyl,
 alkoxy, -CO-alk, hydroxyl, -COOR₅, formyl,
 trifluoromethyl, trifluoromethylsulfanyl,
 20 trifluoromethoxy, nitro, -NR₆R₇, -CO-NH-NR₆R₇,

-N(alk)COOR₈, cyano, -CONHR₉, -CO-NR₁₆R₁₇,
alkylsulfanyl, hydroxyalkyl, -O-alk-NR₁₂R₁₃ or
alkylthioalkyl; or heteroaryl chosen from
benzofuryl, benzothiazolyl, benzothienyl,
5 benzoxazolyl, chromanyl,
2,3-dihydrobenzofuryl, 2,3-
dihydrobenzothienyl, indolinyl, indolyl,
isochromanyl, isoquinolyl, pyridyl, quinolyl,
1,2,3,4-tetrahydroisoquinolyl,
10 1,2,3,4-tetrahydroquinolyl, thiazolyl and
thienyl, wherein the heteroaryl being
unsubstituted or substituted by a halogen,
alkyl, alkoxy, -COOR₅, trifluoromethyl,
trifluoromethylsulfanyl, trifluoromethoxy,
15 nitro, -NR₆R₇, -CO-NH-NR₆R₇, cyano, -CONHR₉,
alkylsulfanyl, hydroxyalkyl or alkylthioalkyl,
R₃ and R₄, which are identical or different,
independently are aryl chosen from phenyl,
naphthyl or indenyl, wherein the aryl being
20 unsubstituted or substituted by one or more
halogen, alkyl, alkoxy, formyl, hydroxyl,
trifluoromethyl, trifluoromethoxy, -CO-alk,
cyano, -COOR₅, -CONR₁₀R₁₁, -CO-NH-NR₆R₇,
alkylsulfanyl, hydroxyalkyl, -alk-NR₆R₇ or
25 alkylthioalkyl; or heteroaryl chosen from
benzofuryl, benzothiazolyl, benzothienyl,
benzoxazolyl, chromanyl, 2,3-

5 dihydrobenzofuryl, 2,3-dihydrobenzothienyl,
furyl, isochromanyl, isoquinolyl, pyrrolyl,
quinolyl, 1,2,3,4-tetrahydroisoquinolyl,
thiazolyl and thienyl, wherein the heteroaryl
being unsubstituted or substituted by a
halogen, alkyl, alkoxy, hydroxyl,
trifluoromethyl, trifluoromethoxy, cyano,
-COOR₅, -CO-NH-NR₆R₇, -CONR₁₀R₁₁, -alk-NR₆R₇,
alkylsulfanyl, hydroxyalkyl or alkylthioalkyl;
10 R₅ is alkyl or phenyl optionally substituted by one
or more halogens,
R₆ and R₇, which are identical or different,
independently are hydrogen, alkyl, -COOalk,
cycloalkyl, alkylcycloalkyl, -alk-O-alk or
15 hydroxyalkyl; or
R₆ and R₇ taken together with the nitrogen atom to
which they are attached form a saturated or
unsaturated and mono- or bicyclic heterocycle
having 3 to 10 ring members optionally
20 comprising another heteroatom chosen from
oxygen, sulfur and nitrogen and optionally
being substituted by one or more alkyl,
-COalk, -COOalk, -CO-NHalk, -CS-NHalk, -CO-
alk-NR₁₄R₁₅, oxo, hydroxyalkyl, -alk-O-alk or
25 -CO-NH₂ radicals;
R₈ is alkyl;

- R_9 is hydrogen, alkyl or alkyl substituted by dialkylamino, phenyl, cycloalkyl (optionally substituted by -COOalk) or a saturated or unsaturated and mono- or bicyclic heterocycle having 3 to 10 ring members optionally comprising one or more heteroatoms chosen from oxygen, sulfur and nitrogen and optionally being substituted by one or more alkyl radicals;
- R_{10} and R_{11} , which are identical or different, independently are hydrogen or alkyl; or R_{10} and R_{11} taken together with the nitrogen atom to which they are attached form a saturated mono- or bicyclic heterocycle having 3 to 10 ring members optionally comprising another heteroatom chosen from oxygen, sulfur and nitrogen and optionally being substituted by alkyl;
- R_{12} and R_{13} , which are identical or different, independently are hydrogen, alkyl or cycloalkyl; or R_{12} and R_{13} taken together with the nitrogen atom to which they are attached form a saturated mono- or bicyclic heterocycle having 3 to 10 ring members optionally comprising another heteroatom chosen from oxygen, sulfur and nitrogen and optionally being substituted by

an alkyl, -COalk, -COOalk, -CO-NHalk,
-CS-NHalk or -CO-alk-NR₁₄R₁₅ or a saturated
mono- or bicyclic heterocycle having 3 to 10
ring members and comprising a heteroatom
5 chosen from oxygen, sulfur and nitrogen,
R₁₄ and R₁₅, which are identical or different,
independently are hydrogen, alkyl or -COOalk;
R₁₆ and R₁₇ taken together with the nitrogen atom to
which they are attached form a saturated mono-
10 or bicyclic heterocycle having 3 to 10 ring
members optionally comprising another
heteroatom chosen from oxygen, sulfur and
nitrogen;
R' is hydrogen or -CO-alk;
15 alk is an alkyl or alkylene radical;
it being understood that the alkyl and alkylene
radicals and portions and the alkoxy radicals
and portions have straight or branched chains
and comprise 1 to 6 carbon atoms; or
20 an optical isomer or an enantiomer or a
diastereoisomer thereof or a pharmaceutically
acceptable salt thereof.

2. The combination according to claim 1, wherein the
25 compound of formula (I) as defined in claim 1 is
chosen from the following compounds:

1-benzhydryl-3-[(methylsulfonyl)(phenyl)-
methylene]azetidine,
1-benzhydryl-3-[(3-methylphenyl)(methylsulfonyl)-
methylene]azetidine,
5 1-benzhydryl-3-[(3-chlorophenyl)(methylsulfonyl)-
methylene]azetidine,
1-benzhydryl-3-[(3,5-dichlorophenyl)-
(methylsulfonyl)-methylene]azetidine,
1-benzhydryl-3-[(2,5-dichlorophenyl)-
10 (methylsulfonyl)-methylene]azetidine,
1-benzhydryl-3-[(2,3-dichlorophenyl)-
(methylsulfonyl)-methylene]azetidine,
1-benzhydryl-3-[(3-fluorophenyl)(methylsulfonyl)-
methylene]azetidine,
15 1-benzhydryl-3-[(3,5-difluorophenyl)-
(methylsulfonyl)-methylene]azetidine,
1-benzhydryl-3-[(3-bromophenyl)(methylsulfonyl)-
methylene]azetidine,
1-benzhydryl-3-[(3-iodophenyl)(methylsulfonyl)-
20 methylene]azetidine,
1-benzhydryl-3-[(methylsulfonyl)(3-trifluoro-
methoxyphenyl)methylene]azetidine,
1-benzhydryl-3-[(methylsulfonyl)(3-trifluoro-
methylphenyl)methylene]azetidine,
25 1-benzhydryl-3-[[3,5-bis(trifluoromethyl)phenyl]-
(methylsulfonyl)methylene]azetidine,

1-benzhydryl-3-[(3,5-dibromophenyl)-(methysulfonyl)-methylene]azetidine,
1-benzhydryl-3-[(3-methoxycarbonylphenyl)-(methysulfonyl)methylene]azetidine,
5 1-benzhydryl-3-[(3-cyanophenyl)(methysulfonyl)-methylene]azetidine,
1-benzhydryl-3-[(3-carbamoylphenyl)-(methysulfonyl)-methylene]azetidine,
1-benzhydryl-3-[(methysulfonyl)(naphth-1-yl)(methysulfonyl)methylene]azetidine,
10 1-[bis(4-chlorophenyl)methyl]-3-[(3,5-difluorophenyl)(methysulfonyl)methylene]azetidine,
1-[bis(4-methoxyphenyl)methyl]-3-[(3,5-difluorophenyl)(methysulfonyl)methylene]azetidine,
15 1-[bis(4-methylphenyl)methyl]-3-[(3,5-difluorophenyl)(methysulfonyl)methylene]azetidine,
(RS)-3-[(3,5-difluorophenyl)(methysulfonyl)-methylene]-1-[(4-methoxyphenyl)(phenyl)methyl]-azetidine,
20 (R)-3-[(3,5-difluorophenyl)(methysulfonyl)-methylene]-1-[(4-methoxyphenyl)(phenyl)methyl]-azetidine,
(S)-3-[(3,5-difluorophenyl)(methysulfonyl)-methylene]-1-[(4-methoxyphenyl)(phenyl)methyl]-azetidine,
25 1-[bis(4-trifluoromethoxyphenyl)methyl]-3-[(3,5-difluorophenyl)(methysulfonyl)methylene]-azetidine,

1-[bis(4-trifluoromethylphenyl)methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
1-[bis(4-chlorophenyl)methyl]-3-[(3,5-bis(trifluoro-methyl)phenyl)(methylsulfonyl)-
5 methylene]azetidine,
(RS)-1-[(4-chlorophenyl)(2,4-dichlorophenyl)methyl]-3-[(3,5-difluorophenyl)-(methylsulfonyl)-methylene]azetidine,
(R)-1-[(4-chlorophenyl)(2,4-dichlorophenyl)-
10 methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)-methylene]azetidine,
(S)-1-[(4-chlorophenyl)(2,4-dichlorophenyl)-methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)-methylene]azetidine,
15 (RS)-1-[(4-chlorophenyl)[4-(hydroxymethyl)phenyl]-methyl]-3-[(3,5-difluoro-phenyl)(methylsulfonyl)-methylene]azetidine,
(R)-1-[(4-chlorophenyl)[4-(hydroxymethyl)phenyl]-methyl]-3-[(3,5-difluoro-phenyl)(methylsulfonyl)-
20 methylene]azetidine,
(S)-1-[(4-chlorophenyl)[4-(hydroxymethyl)phenyl]-methyl]-3-[(3,5-difluoro-phenyl)(methylsulfonyl)-methylene]azetidine,
(RS)-1-[(4-chlorophenyl)[4-(pyrrolidinylmethyl)-
25 phenyl]methyl]-3-[(3,5-difluoro-phenyl)(methylsulfonyl)methylene]azetidine,

(R)-1-{{(4-chlorophenyl)[4-(pyrrolidinylmethyl)-phenyl]methyl}-3-[(3,5-difluoro-phenyl)(methylsulfonyl)methylene]azetidine,
(S)-1-{{(4-chlorophenyl)[4-(pyrrolidinylmethyl)-phenyl]methyl}-3-[(3,5-difluoro-phenyl)(methylsulfonyl)methylene]azetidine,
5 1-{{(RS)-(4-chlorophenyl)[4-(3,3-dimethylpiperidin-1-ylmethyl)phenyl]methyl}-3-[(3,5-difluoro-phenyl)(methylsulfonyl)methylene]azetidine,
10 1-{{(R)-(4-chlorophenyl)[4-(3,3-dimethylpiperidin-1-ylmethyl)phenyl]methyl}-3-[(3,5-difluoro-phenyl)(methylsulfonyl)methylene]azetidine,
1-{{(S)-(4-chlorophenyl)[4-(3,3-dimethylpiperidin-1-ylmethyl)phenyl]methyl}-3-[(3,5-difluoro-phenyl)(methylsulfonyl)methylene]azetidine,
15 1-{{(RS)-(4-chlorophenyl)[4-(thiomorpholin-4-ylmethyl)phenyl]methyl}-3-[(3,5-difluoro-phenyl)(methylsulfonyl)methylene]azetidine,
1-{{(R)-(4-chlorophenyl)[4-(thiomorpholin-4-ylmethyl)phenyl]methyl}-3-[(3,5-difluoro-phenyl)(methylsulfonyl)methylene]azetidine,
20 1-{{(S)-(4-chlorophenyl)[4-(thiomorpholin-4-ylmethyl)phenyl]methyl}-3-[(3,5-difluoro-phenyl)(methylsulfonyl)methylene]azetidine,
25 1-{{(RS)-(4-chlorophenyl)[4-(N-ethyl-N-cyclohexylaminomethyl)phenyl]methyl}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,

1-{{(R)-(4-chlorophenyl)[4-(N-ethyl-N-cyclohexylaminomethyl)phenyl]methyl}}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
1-{{(S)-(4-chlorophenyl)[4-(N-ethyl-N-cyclohexylaminomethyl)phenyl]methyl}}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
5 1-{{(RS)-(4-chlorophenyl){4-[(4-ethoxycarbonylpiperazinyl)methyl]phenyl}methyl}}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
10 1-{{(R)-(4-chlorophenyl){4-[(4-ethoxycarbonylpiperazinyl)methyl]phenyl}methyl}}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
1-{{(S)-(4-chlorophenyl){4-[(4-ethoxycarbonylpiperazinyl)methyl]phenyl}methyl}}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
15 1-{{(RS)-(4-chlorophenyl)[4-(N-cyclopropyl-N-propylaminomethyl)phenyl]methyl}}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
1-{{(R)-(4-chlorophenyl)[4-(N-cyclopropyl-N-propylaminomethyl)phenyl]methyl}}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
20 1-{{(S)-(4-chlorophenyl)[4-(N-cyclopropyl-N-propylaminomethyl)phenyl]methyl}}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
25 1-{{(RS)-(4-chlorophenyl)[4-(diisopropylaminomethyl)phenyl]methyl}}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,

1-{(R)-(4-chlorophenyl)[4-(diisopropylaminomethyl)-
phenyl]methyl}-3-[(3,5-difluorophenyl)(methyl-
sulfonyl)methylene]azetidine,
1-{(S)-(4-chlorophenyl)[4-(diisopropylaminomethyl)-
phenyl]methyl}-3-[(3,5-difluorophenyl)(methyl-
sulfonyl)methylene]azetidine,
1-{{{(RS)-(4-chlorophenyl){4-[bis(2-methoxyethyl)-
aminomethyl]phenyl}methyl}}}-3-[(3,5-
difluorophenyl)(methylsulfonyl)methylene]azetidine,
1-{{{(R)-(4-chlorophenyl){4-[bis(2-methoxyethyl)-
aminomethyl]phenyl}methyl}}}-3-[(3,5-
difluorophenyl)(methylsulfonyl)methylene]azetidine,
1-{{{(S)-(4-chlorophenyl){4-[bis(2-methoxyethyl)-
aminomethyl]phenyl}methyl}}}-3-[(3,5-
difluorophenyl)(methylsulfonyl)methylene]azetidine,
1-{(RS)-(4-chlorophenyl)[4-(di(n-
propyl)aminomethyl)phenyl]methyl}-3-[(3,5-difluoro-
phenyl)(methylsulfonyl)methylene]azetidine,
1-{(R)-(4-chlorophenyl)[4-(di(n-
propyl)aminomethyl)phenyl]methyl}-3-[(3,5-
difluorophenyl)(methylsulfonyl)methylene]azetidine,
1-{(S)-(4-chlorophenyl)[4-(di(n-
propyl)aminomethyl)phenyl]methyl}-3-[(3,5-
difluorophenyl)(methylsulfonyl)methylene]azetidine,
1-{(RS)-(4-chlorophenyl)[4-(piperidin-1-ylmethyl)-
phenyl]methyl}-3-[(3,5-difluorophenyl)(methyl-
sulfonyl)methylene]azetidine,

- 1-{(R)-(4-chlorophenyl)[4-(piperidin-1-ylmethyl)-phenyl]methyl}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
- 1-{(S)-(4-chlorophenyl)[4-(piperidin-1-ylmethyl)-phenyl]methyl}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
- 1-{(RS)-(4-chlorophenyl)[4-(4-methylpiperazin-1-ylmethyl)phenyl]methyl}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
- 1-{(R)-(4-chlorophenyl)[4-(4-methylpiperazin-1-ylmethyl)phenyl]methyl}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
- 1-{(S)-(4-chlorophenyl)[4-(4-methylpiperazin-1-ylmethyl)phenyl]methyl}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
- 1-{(RS)-(4-chlorophenyl)[4-(morpholin-4-ylmethyl)phenyl]methyl}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
- 1-{(R)-(4-chlorophenyl)[4-(morpholin-4-ylmethyl)-phenyl]methyl}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
- 1-{(S)-(4-chlorophenyl)[4-(morpholin-4-ylmethyl)-phenyl]methyl}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
- 1-{(RS)-(4-chlorophenyl)[4-(diethylaminomethyl)-phenyl]methyl}-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,

1-{(R)-(4-chlorophenyl)[4-(diethylaminomethyl)-
phenyl]methyl}-3-[(3,5-difluorophenyl)(methyl-
sulfonyl)methylene]azetidine,
1-{(S)-(4-chlorophenyl)[4-(diethylaminomethyl)-
phenyl]methyl}-3-[(3,5-difluorophenyl)(methyl-
sulfonyl)methylene]azetidine,
1-{(RS)-(4-chlorophenyl)[4-(piperazin-2-one-4-
ylmethyl)phenyl]methyl}-3-[(3,5-
difluorophenyl)(methylsulfonyl)methylene]azetidine,
1-{(R)-(4-chlorophenyl)[4-(piperazin-2-one-4-
ylmethyl)phenyl]methyl}-3-[(3,5-
difluorophenyl)(methylsulfonyl)methylene]azetidine,
1-{(S)-(4-chlorophenyl)[4-(piperazin-2-one-4-
ylmethyl)phenyl]methyl}-3-[(3,5-
difluorophenyl)(methylsulfonyl)methylene]azetidine,
1-{(RS)-(4-chlorophenyl)[4-(imidazol-1-ylmethyl)-
phenyl]methyl}-3-[(3,5-difluorophenyl)(methyl-
sulfonyl)methylene]azetidine,
1-{(R)-(4-chlorophenyl)[4-(imidazol-1-ylmethyl)-
phenyl]methyl}-3-[(3,5-difluorophenyl)(methyl-
sulfonyl)methylene]azetidine,
1-{(S)-(4-chlorophenyl)[4-(imidazol-1-ylmethyl)-
phenyl]methyl}-3-[(3,5-difluorophenyl)(methyl-
sulfonyl)methylene]azetidine,
(RS)-1-[(4-chlorophenyl)[4-(N,N-
dimethylcarbamoyl)phenyl]methyl}-3-[(3,5-
difluorophenyl)(methylsulfonyl)methylene]azetidine,

(R)-1-[(4-chlorophenyl)[4-(N,N-dimethylcarbamoyl)phenyl]methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
(S)-1-[(4-chlorophenyl)[4-(N,N-dimethylcarbamoyl)phenyl]methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
5 (RS)-1-[(4-chlorophenyl)[4-(N-ethylcarbamoyl)phenyl]methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
10 (R)-1-[(4-chlorophenyl)[4-(N-ethylcarbamoyl)phenyl]methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
(S)-1-[(4-chlorophenyl)[4-(N-ethylcarbamoyl)phenyl]methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
15 (RS)-1-[(4-carbamoylphenyl)(4-chlorophenyl)methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
(R)-1-[(4-carbamoylphenyl)(4-chlorophenyl)methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
20 (S)-1-[(4-carbamoylphenyl)(4-chlorophenyl)methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
25 1-[bis(4-chlorophenyl)methyl]-3-[(3,5-dichlorophenyl)(methylsulfonyl)methylene]azetidine,

- 1-benzhydryl-3-[(3-methylsulfanylphenyl)(methylsulfonyl)methylene]azetidine,
1-benzhydryl-3-[(3-methylsulfanylmethyl)phenyl]-(methylsulfonyl)methylene]azetidine,
5 1-[bis(4-chlorophenyl)methyl]-3-[(3-cyanophenyl)-(methylsulfonyl)methylene]azetidine,
1-[bis(4-chlorophenyl)methyl]-3-[(3-carbamoylphenyl)(methylsulfonyl)methylene]azetidine,
10 1-[bis(4-chlorophenyl)methyl]-3-[(3-methoxyphenyl)-(methylsulfonyl)methylene]azetidine,
1-[bis(4-chlorophenyl)methyl]-3-[(3-hydroxyphenyl)-(methylsulfonyl)methylene]azetidine,
1-[bis(4-chlorophenyl)methyl]-3-[(methylsulfonyl)-(3-pyrrolidinylphenyl)methylene]azetidine,
15 1-[bis(4-chlorophenyl)methyl]-3-[(3-hydroxymethylphenyl)(methylsulfonyl)methylene]azetidine,
1-[bis(4-chlorophenyl)methyl]-3-{(methylsulfonyl)[3-(N-piperidinylcarbamoyl)phenyl]methylene}azetidine,
20 1-[bis(4-chlorophenyl)methyl]-3-[(methylsulfonyl)(3-trifluoromethylsulfanylphenyl)-(methylsulfonyl)methylene]azetidine,
1-[bis(4-fluorophenyl)methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
25 1-[bis(2-fluorophenyl)methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,

1-[bis(3-fluorophenyl)methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
(RS)-1-[(4-chlorophenyl)(thiazol-2-yl)methyl]-3-[(methylsulfonyl)(phenyl)methylene]azetidine,
5 (R)-1-[(4-chlorophenyl)(thiazol-2-yl)methyl]-3-[(methylsulfonyl)(phenyl)methylene]azetidine,
(S)-1-[(4-chlorophenyl)(thiazol-2-yl)methyl]-3-[(methylsulfonyl)(phenyl)methylene]azetidine,
(RS)-1-[(4-chlorophenyl)(thien-2-yl)methyl]-3-
10 [(3,5-difluorophenyl)(methylsulfonyl)methylene]-azetidine,
(R)-1-[(4-chlorophenyl)(thien-2-yl)methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
(S)-1-[(4-chlorophenyl)(thien-2-yl)methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine,
15 1-benzhydryl-3-[(ethylsulfonyl)(phenyl)methylene]-azetidine,
1-[bis(4-chlorophenyl)methyl]-3-{{3-[N-(4-methylpiperazinyl)carbamoyl]phenyl}(methylsulfonyl)methylene}azetidine,
20 1-[bis(4-chlorophenyl)methyl]-3-{{3-(2,2-dimethylcarbohydrazido)phenyl}(methylsulfonyl)methylene}azetidine,
1-[bis(thien-2-yl)methyl]-3-[(3,5-difluorophenyl)-(methylsulfonyl)methylene]azetidine,
25 1-[bis(p-tolyl)methyl]-3-[(methylsulfonyl)-(phenyl)methylene]azetidine,

1-[(4-chlorophenyl)(4-hydroxymethylphenyl)methyl]-
3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]-
azetidine,
1-[bis(4-chlorophenyl)methyl]-3-[(3-
5 methylaminophenyl)-
(methylsulfonyl)methylene]azetidine,
(RS)-1-[(4-chlorophenyl)(thiazol-2-yl)methyl]-3-
[(3,5-difluorophenyl)(methylsulfonyl)methylene]-
azetidine,
10 (R)-1-[(4-chlorophenyl)(thiazol-2-yl)methyl]-3-
[(3,5-difluorophenyl)(methylsulfonyl)methylene]-
azetidine,
(S)-1-[(4-chlorophenyl)(thiazol-2-yl)methyl]-3-
[(3,5-difluorophenyl)(methylsulfonyl)methylene]-
15 azetidine,
1-[bis(4-chlorophenyl)methyl]-3-
[(methylsulfonyl)(2-methoxycarbonylthien-5-
yl)methylene]azetidine,
(RS)-1-[bis(4-chlorophenyl)methyl]-3-hydroxy-3-
20 [(methylsulfonyl)(2-methoxycarbonylthien-5-
yl)methyl]azetidine,
1-[bis(4-chlorophenyl)methyl]-3-[(2-isobutylamino-
carbonylthien-5-yl)(methylsulfonyl)methylene]-
azetidine,
25 1-[bis(4-chlorophenyl)methyl]-3-[(RS)-(3-methoxy-
carbonylphenyl)(methylsulfonyl)methyl]azetidin-3-
ol,

1-[bis(4-chlorophenyl)methyl]-3-[(RS)-(methylsulfonyl)(pyridin-4-yl)methyl]azetidin-3-ol,
1-[bis(4-chlorophenyl)methyl]-3-[(RS)-(methylsulfonyl)(pyridin-3-yl)methyl]azetidin-3-ol,
5 3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-(3-(morpholin-4-yl)propyl)benzamide,
3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-(3-
10 dimethylaminopropyl)benzamide,
3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-(2-(pyrrolidin-1-yl)ethyl)benzamide,
3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-(2-
15 dimethylamino-1-methylethyl)benzamide,
3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-(piperidin-1-yl)benzamide,
20 3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-isobutylbenzamide,
3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-(3-(imidazol-1-yl)propyl)benzamide,
25

3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-(2-dimethylaminoethyl)benzamide,
N'-methylhydrazide of 3-({1-[bis(4-chlorophenyl)-
5 methyl]azetidin-3-ylidene}(methanesulfonyl)-methyl)benzoic acid,
3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-(2-(morpholin-4-yl)ethyl)benzamide,
10 3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-(1-ethylpyrrolidin-2-ylmethyl)benzamide,
3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-(2,2-
15 dimethylpropyl)benzamide,
3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-(cyclohexylmethyl)benzamide,
3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-
20 ylidene}(methanesulfonyl)methyl)-N-(cyclopropylmethyl)benzamide,
3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-(2-methylbutyl)benzamide,
25 3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-(2-phenylpropyl)benzamide,

3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-(tetrahydrofuran-2-ylmethyl)benzamide,
3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-(2,2-diphenylethyl)benzamide,
3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-N-(2-ethylbutyl)benzamide,
methyl ester of 4-{[3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-benzoylamino]methyl}cyclohexanecarboxylic acid,
2-amino-1-{4-[3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)phenyl]-piperazin-1-yl}ethanone,
tert-butyl ester of (2-{4-[3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)phenyl]piperazin-1-yl}-2-oxoethyl)carbamic acid,
1-{4-[3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)phenyl]piperazin-1-yl}-2-(methylamino)ethanone,
tert-butyl ester of (2-{4-[3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)phenyl]piperazin-1-yl}-2-oxoethyl)-N-methylcarbamic acid,

N-methylamide of 4-[3-({1-[bis(4-chlorophenyl)-
methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-
phenyl]piperazine-1-carbothioic acid,
N-methylamide of 4-[3-({1-[bis(4-
5 chlorophenyl)methyl]azetidin-3-
ylidene}(methanesulfonyl)methyl)phenyl]piperazine-
1-carboxylic acid,
methyl ester of 4-[3-({1-[bis(4-
chlorophenyl)methyl]azetidin-3-
10 ylidene}(methanesulfonyl)methyl)phenyl]piperazine-
1-carboxylic acid,
1-[3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-
ylidene}(methanesulfonyl)methyl)phenyl]-4-
isobutylpiperazine,
15 1-[3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-
ylidene}(methanesulfonyl)methyl)phenyl]-4-
ethylpiperazine,
4-acetyl-1-[3-({1-[bis(4-
chlorophenyl)methyl]azetidin-3-
20 ylidene}(methanesulfonyl)methyl)phenyl]piperazine,
1-{4-[3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-
ylidene}(methanesulfonyl)methyl)phenyl]piperazin-1-
yl}-2-dimethylaminoethanone,
1-[3-({1-[bis(4-chlorophenyl)methyl]azetidin-3-
25 ylidene}(methanesulfonyl)methyl)phenyl]piperazine,

tert-butyl ester of 4-[3-({1-[bis(4-chlorophenyl)-
methyl]azetidin-3-ylidene}(methanesulfonyl)methyl)-
phenyl]piperazine-1-carboxylic acid,
1-[bis(4-methoxycarbonylphenyl)methyl]-3-[(3,5-
5 difluorophenyl)(methysulfonyl)methylene]azetidine,
3-acetoxy-1-[bis(4-methoxycarbonylphenyl)methyl]-3-
[(RS)-(3,5-difluorophenyl)(methysulfonyl)methyl]-
azetidine,
(RS)-4-[4-((4-chlorophenyl){3-[(3,5-
10 difluorophenyl)(methanesulfonyl)methylene]azetidin-
1-yl)methyl}benzyl)morpholine,
4-(4-{3-[(1-benzhydrylazetidin-3-ylidene)(methane-
sulfonyl)methyl]phenoxy}butyl)morpholine,
4-(4-{3-[(1-benzhydrylazetidin-3-ylidene)(methane-
15 sulfonyl)methyl]phenoxy}propyl)morpholine,
their optical isomers and their pharmaceutically
acceptable salts.

3. The combination according to claim 1, wherein the
20 compound of formula (I) as defined in claim 1 is
1-[bis(4-chlorophenyl)methyl]-3-[(3,5-
difluorophenyl)(methysulfonyl)methylene]-
azetidine),
or a pharmaceutically acceptable salt thereof.

25

4. The combination according to claim 1, wherein the
product which activates dopaminergic

neurotransmission in the brain is chosen from the following compounds:

bromocriptine, cabergoline, adrogolide, BAM-1110, duodopa, levodopa, dopadose, CHF1512, PNU-95666, ropinirole, pramipexole, rotigotine, spheramine, TV1203, uridine, rasagiline, selegiline, SL340026, tolcapone and entacapone.

5. The combination according to claim 1, wherein the product which activates dopaminergic neurotransmission in the brain is levodopa and the CB1 antagonist is 1-[bis(4-chlorophenyl)methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]-azetidine).
6. The combination according to claim 1, wherein the product which activates dopaminergic neurotransmission in the brain is ropinirole and the CB1 antagonist is 1-[bis(4-chlorophenyl)methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]azetidine).
7. The combination according to claim 1, wherein the product which activates dopaminergic neurotransmission in the brain is bromocriptine and the CB1 antagonist is 1-[bis(4-chloro-

phenyl)methyl]-3-[(3,5-difluorophenyl)-(methysulfonyl)methylene]azetidine).

8. The combination according to claim 1, wherein the
5 product which activates dopaminergic neurotransmission in the brain is pramipexole and the CB1 antagonist is 1-[bis(4-chlorophenyl)methyl]-3-[(3,5-difluorophenyl)-(methysulfonyl)methylene]azetidine).
- 10 9. The combination according to claim 1, wherein the product which activates dopaminergic neurotransmission in the brain is rasagiline and the CB1 antagonist is 1-[bis(4-chlorophenyl)methyl]-3-[(3,5-difluorophenyl)-(methysulfonyl)methylene]azetidine).
- 15 10. The combination according to claim 1, wherein the product which activates dopaminergic neurotransmission in the brain is entacapone and the CB1 antagonist is 1-[bis(4-chlorophenyl)methyl]-3-[(3,5-difluorophenyl)-(methysulfonyl)methylene]azetidine).
- 20 11. A method of treating Parkinson's disease in a patient comprising administering to said patient a therapeutically effective amount of a combination of a product which activates dopaminergic
- 25

neurotransmission in the brain and one or more CB1 antagonists of formula (I) as defined in claim 1, optionally in combination with a pharmaceutically acceptable carrier.

5

12. The method according to claim 11, wherein the compound of formula (I) as defined in claim 1 is 1-[bis(4-chlorophenyl)methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]-azetidine),
or a pharmaceutically acceptable salt thereof.

10

13. The method according to claim 11, wherein the product which activates dopaminergic neurotransmission in the brain is chosen from the following compounds:

15

bromocriptine, cabergoline, adrogolide, BAM-1110, duodopa, levodopa, dopadose, CHF1512, PNU-95666, ropinirole, pramipexole, rotigotine, speramine, TV1203, uridine, rasagiline, selegiline, SL340026, tolcapone and entacapone.

20

14. The method according to claim 11, wherein said product and said compound of formula (I) as defined in claim 1 are administered either simultaneously, separately or spread out over time.

25

15. A pharmaceutical composition comprising one or more products which activate dopaminergic neurotransmission in the brain and one or more CB1 antagonist of formula (I) as defined in claim 1 in combination with a compatible and pharmaceutically acceptable vehicle.
16. The pharmaceutical composition according to claim 15, wherein the compound of formula (I) as defined in claim 1 is 1-[bis(4-chlorophenyl)methyl]-3-[(3,5-difluorophenyl)(methylsulfonyl)methylene]-azetidine), or a pharmaceutically acceptable salt thereof.
17. The pharmaceutical composition according to claim 15, wherein the product which activates dopaminergic neurotransmission in the brain is chosen from the following compounds:
bromocriptine, cabergoline, talipexole, adrogolide, BAM-1110, duodopa, levodopa, dopadose, CHF1512, PNU-95666, ropinirole, pramipexole, rotigotine, spheramine, TV1203, uridine, rasagiline, selegiline, SL340026, tolcapone and entacapone.
18. The pharmaceutical composition according to claim 15, wherein the product which activates dopaminergic neurotransmission in the brain is

levodopa and the CB1 antagonist is 1-[bis(4-chlorophenyl)methyl]-3-[(3,5-difluorophenyl)-(methylsulfonyl)methylene]azetidine).

5 19. The pharmaceutical composition according to claim
15, wherein the product which activates
dopaminergic neurotransmission in the brain is
ropinirole and the CB1 antagonist is
1-[bis(4-chlorophenyl)methyl]-3-[(3,5-
10 difluorophenyl)(methylsulfonyl)methylene]-
azetidine).

20. The pharmaceutical composition according to claim
15, wherein the product which activates
dopaminergic neurotransmission in the brain is
bromocriptine and the CB1 antagonist is
1-[bis(4-chlorophenyl)methyl]-3-[(3,5-
15 difluorophenyl)(methylsulfonyl)methylene]-
azetidine).

20
21. The pharmaceutical composition according to claim
15, wherein the product which activates
dopaminergic neurotransmission in the brain is
pramipexole and the CB1 antagonist is
25 1-[bis(4-chlorophenyl)methyl]-3-[(3,5-
difluorophenyl)(methylsulfonyl)methylene]-
azetidine).

22. The pharmaceutical composition according to claim
15, wherein the product which activates
dopaminergic neurotransmission in the brain is
rasagiline and the CB1 antagonist is
5 1-[bis(4-chlorophenyl)methyl]-3-[(3,5-
difluorophenyl)(methylsulfonyl)methylene]-
azetidine).
23. The pharmaceutical composition according to claim
10 15, wherein the product which activates
dopaminergic neurotransmission in the brain is
entacapone and the CB1 antagonist is
1-[bis(4-chlorophenyl)methyl]-3-[(3,5-
difluorophenyl)(methylsulfonyl)methylene]-
15 azetidine).
24. The pharmaceutical composition according to claim
15, wherein the CB1 antagonist of formula (I) as
defined in claim 1 is present in an amount of from
20 about 0.1 mg to about 500 mg.